POPULATION HEALTH MANAGEMENT
Volume 17, Number 2, 2014

DOI: 10.1089/pop.2013.0041

Treating Pain in Addicted Patients: Recommendations from an Expert Panel

Martin Cheatle, PhD,[1] Dominique Comer, PharmD,[2] Martha Wunsch, MD,[3] Alexis Skoufalos, EdD,[2] and Yeshwant Reddy, MD[4]

Abstract

Clinicians may face pragmatic, ethical, and legal issues when treating addicted patients. Equal pressures exist for clinicians to always address the health care needs of these patients in addition to their addiction. Although controversial, mainly because of the lack of evidence regarding their long-term efficacy, the use of opioids for the treatment of chronic pain management is widespread. Their use for pain management in the addicted population can present even more challenges, especially when evaluating the likelihood of drug-seeking behavior. As the misuse and abuse of opioids continues to burgeon, clinicians must be particularly vigilant when prescribing chronic opioid therapy. The purpose of this article is to summarize recommendations from a recent meeting of experts convened to recommend how primary care physicians should approach treatment of chronic pain for addicted patients when an addiction specialist is not available for a referral. As there is a significant gap in guidelines and recommendations in this specific area of care, this article serves to create a foundation for expanding chronic pain guidelines in the area of treating the addicted population. This summary is designed to be a practical how-to guide for primary care physicians, discussing risk assessment, patient stratification, and recommended therapeutic approaches. (*Population Health Management* 2014;17:79–89)

Introduction

When treating patients who have a known addiction or have drug-seeking behaviors, clinicians may face pragmatic, ethical, and legal issues. At times, distinguishing between true addiction, physical dependence, and pseudoaddiction can be challenging, yet equal pressure exists for clinicians to always address the health care needs of the patient.[1] Although controversial, mainly because of the lack of evidence regarding their long-term efficacy,[2] the use of opioids for the treatment of chronic pain management is widespread. Their use for pain management in the addicted population can present even more challenges, especially when evaluating the likelihood of drug-seeking behavior.[1] This is particularly onerous for primary care physicians (PCPs), who are responsible for providing pain care to more than half of all chronic pain patients.[3] The majority of these PCPs do not have the time or training in pain medicine or addiction to effectively assess and manage these complex patients.[4] Further complicating the addicted patient receiving care are certain barriers, such as the stigma of being labeled as drug seeking or an addict, which encourage an afflicted patient to hide his or her addiction. Common misconceptions about pain and substance use disorders, such as tolerance for and dependence on prescribed opioids as signs of addiction, can further complicate optimal care.[5] Another barrier is access, as more than 50% of patients do not seek mental health care because of cost.[6]

As the misuse and abuse of opioids continues to burgeon, clinicians must be particularly vigilant when prescribing chronic opioid therapy (COT).[7] For example, Ives et al evaluated opioid misuse in 196 patients with chronic noncancer pain (CNCP). They discovered that 32% of this population engaged in opioid misuse as defined by inappropriate results from urine drug screening; 40.3% of the opioid misusers were positive for cocaine or amphetamines in the urine drug screen, while 24.2% had a negative urine drug screen for the prescribed opioid, and 18% showed positive for cannabinoids.[8] A study completed by Fishbain et al found that among those receiving COT for CNCP, the abuse/addiction rate was 3.27% and aberrant drug-related behavior (ADRB) was 11.5%. With respect to urine drug

[1]University of Pennsylvania Center for Studies of Addiction, Philadelphia, PA.
[2]Jefferson School of Population Health, Philadelphia, PA.
[3]The TASL Clinic, Blackburg, VA.
[4]Neurological Associates, Columbus, OH.

testing, 20.4% returned negative for the prescribed opioid, and illicit drugs were discovered in 14.5% of cases.[9] Using the more sensitive *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5), criteria for prescription opioid use disorders, Boscarino et al evaluated 705 patients with CNCP who were receiving COT. Based on DSM-5, 21.7% of these patients met criteria for moderate opioid use disorder and 13.2% also met criteria for severe opioid use disorder.[10]

The purpose of this article is to summarize recommendations from a recent meeting of experts convened to recommend how PCPs should approach treatment of chronic pain for addicted patients when an addiction specialist is not available for a referral. There is a significant gap in guidelines and recommendations in this specific area of care. This article serves to create a foundation for expanding chronic pain guidelines in the area of treating the addicted population. It is designed to be a practical how-to guide for PCPs for day-to-day practice.

A panel of experts gathered via conference call on December 1, 2012 to discuss the current literature, personal experiences, and suggested recommendations for treating chronic pain in the addicted population. The following is a combination of pertinent literature and the conclusions of the expert panel. This article will discuss risk assessment/stratification and the tools currently available, strategies and recommendations for the management of patients, recommended therapeutic approaches, and resources for physicians. Case studies can be found throughout the recommendations to help guide the reader through the recommendations.

Case study I

- A 35-year-old female with a lumbar disc herniation and radiculopathy partially responds to epidural steroid injections. She is prescribed hydrocodone, a short-acting opioid. Routine Urine Drug Test (UDT) confirms metabolites of hydrocodone but also reveals marijuana (cannabis/THC) metabolite. After a single counseling session, she discontinued using cannabis and 2 subsequent UDTs are appropriate. She continues to be functional, including maintaining full-time gainful employment, with administration of intermittent epidural steroid injections, and is taking hydrocodone as prescribed.

Is it medically appropriate to prescribe hydrocodone to this patient? Yes. After discussion of the results of the UDT and clearly stating the expectations of the clinic, the patient seems to be adhering to clinic guidelines and abstaining from marijuana use. If "random" (ie, nonscheduled) UDTs are negative for illicit substances and positive for prescribed hydrocodone, the physician may cautiously continue prescribing an opioid. Additional safeguards to encourage appropriate behavior include more closely spaced visits, prescriptions for smaller numbers of pills, and requesting that the patient come to the office mid prescription for a tally of pills remaining ("pill counts"). Praise for adherence to abstinence is helpful as opposed to simple admonishments regarding the deleterious effects of cannabis. Describing the risk of diversion when the patient is in contact with the illegal source of cannabis also may be helpful. If the patient is abusing other substances, it will come to light through closer monitoring.

Case study II

- A 60-year-old male with lumbar spondylosis and degenerative disc disease does not respond to epidurals, facet injections, and physical therapy. He is not a surgical candidate. He reports improvement in his back and leg pain with the use of Percocet 10. Routine UDT is positive for opioids but does not show oxycodone metabolites; instead, the UDT has hydrocodone metabolites. UDT showed the same results on 3 occasions. The patient denies taking hydrocodone and the pharmacist report and a review of the state prescription monitoring programs (PMPs) confirms only your prescription for Percocet. Specifically, there are no prescriptions for hydrocodone. An inquiry to the laboratory that performed the UDT confirms the results of the tests are accurate.

What are the prescribing physician's options? The patient should be informed that the laboratory results are not consistent with appropriate use of medication. A frank discussion about the puzzling results, with an emphasis on the danger to others of diverting pain medication and your medical-legal responsibilities as a physician, may elicit an explanation of the problem. Remind the patient that you are willing to listen, problem solve, and move forward rather than accuse him or her of not being truthful. However, let the patient know that if this situation cannot be resolved and medications are not taken as directed, continuation of prescribing opioids will not be appropriate. In such a case you would be glad to continue to provide non-opioid treatment to your patient.

Sharing medication with friends and family occurs, particularly as hydrocodone is the most frequently prescribed opioid in the United States[11] and fairly easy to procure legally and illegally. The 2010 and 2011 National Survey on Drug Use and Health reports that among individuals older than age 12 using pain relievers nonmedically, more than half (54.2%) obtained them from a friend or family member for free and 16% bought the medication from a friend or family member. Further, the study showed that diverted medication obtained in this manner came from a physician 81% of the time.[12]

There may be several explanations for the UDT results. An inquiry to the pharmacist can eliminate concerns about potential diversion/substitution at the pharmacy itself. Other scenarios include a family member or caretaker substituting hydrocodone for oxycodone without the patient's knowledge, the patient sharing medication with a family member who is "sicker" and cannot afford oxycodone, or the patient selling medication for money.

As noted in the previous case, additional safeguards to encourage appropriate behavior include more closely spaced visits, prescriptions for smaller numbers of pills, and requests for the patient to come to the office mid prescription for a tally of pills remaining ("pill counts"). Rather than discharging the patient, provide the patient with a 1-day supply of medication with the provision that they return to the clinic the next morning *before* taking their medication. Observe the patient taking the medication and obtain UDT 4 hours after this dose to absolutely confirm the accuracy of the UDT. If the treating physician decides to continue prescribing opiates, the patient can be asked to identify an "approved" support person to safeguard the medication.

A skilled nurse or midlevel provider can interview the support person to determine his or her appropriateness for this role. Obtain consent to communicate with the support person.

Risk Assessment and Stratification

For proper risk assessment and stratification, often-used terminology must be clearly defined:

Addiction:

> Addiction is a primary, chronic disease of brain reward, motivation, memory, and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social, and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.
> Addiction is characterized by inability to consistently abstain, impairment in behavioral control, craving, diminished recognition of significant problems with one's behaviors and interpersonal relationships, and a dysfunctional emotional response. Like other chronic diseases, addiction often involves cycles of relapse and remission. Without treatment or engagement in recovery activities, addiction is progressive and can result in disability or premature death.[13]

It is critical to distinguish addiction from substance abuse or misuse, which are defined as follows:

Abuse:

> A maladaptive pattern of substance use, leading to clinically significant impairment or distress as manifested by 1 or more behaviorally based criteria.[14]

Misuse:

> Incorrect use of a medication by patients, who may use a drug for a purpose other than that for which it was prescribed, combine prescribed medications without the physician's knowledge, take too little or too much of a drug, take it too often, take it for too long, or take it in ways not intended by the prescriber (intranasal, intravenous). Misuse does not apply to off-label prescribing when such use is supported by common medical practice, research, or rational pharmacology.[15]

The use of universal precautions for pain management serves as a good foundation for successful risk assessment and stratification. Physicians must approach all patients in a uniform, systematic way, as the demographics of those who are addicted to, abuse, and misuse medications are changing—and such patients may not always be obvious.[16]

Examples from the expert panel included a middle-aged mother, not employed outside the home, who uses illicitly obtained psychoactive medications to cope or to induce sleep and relieve anxiety; a patient on a fixed income who sells a portion of his or her monthly prescription to meet rising medical bills and other costs of living; and the patient misusing prescribed medication.

Gourlay, Heit, and Almahrezi list the following steps physicians should take as a part of universal precautions for pain management[16]:

- Formulate diagnosis with differentials
- Psychological assessment including risk of addictive disorder
- Informed consent
- Treatment agreement
- Pre- and postintervention assessment of pain level and function
- Trial of opioid therapy and/or adjunctive medication
- Routinely reassess pain score and function
- Regularly assess the "4 A's" (analgesia, activity, adverse effects, aberrant behaviors)
- Periodic review of pain diagnosis and the development of comorbid conditions including addictive disorders
- Documentation

There is some debate regarding the effectiveness of UDT and treatment agreements in curtailing opioid misuse.[17] However, utilizing a treatment agreement allows the clinician the opportunity to establish measurable treatment goals and realistic expectations regarding the use of opioids and other pain management therapies.[18] Although some physicians may feel uncomfortable about asking an established patient to sign a treatment agreement, the expert panel believes that it should be mandatory and a stated policy assures that no one patient or patient type (eg, low income, past history of substance abuse) is singled out. If a patient refuses to sign and it is a clinic policy, the clinician can offer non-opioid therapies (eg, adjunctive medication, physical therapy) or provide a referral to a pain clinic. Informed consent is often mentioned as part of the agreement process but typically is not fully addressed. Informed consent is an important aspect of due diligence in providing opioid therapy and outlines the potential risks of prescription opioid use.[18]

Tools for risk assessment

Consider the following case studies as a guide through the following tools for risk assessment:

Case study III

- Patient is a 45-year-old female with failed back surgery or post-laminectomy syndrome; no further surgical procedures are planned. Patient did not respond to physical therapy and is prescribed gabapentin, cyclobenzaprine, and oxycodone. UDT is negative for illicit substances and positive for prescribed medication. A random pill count suggests that she takes more medications than prescribed and she frequently runs out of her prescribed opiates early.

What is happening here? There are a number of possibilities to consider: incomplete relief of pain because of inadequate dosage (pseudoaddiction or inadequate analgesia); a new diagnosis; worsening of pain generator; tolerance; seeking euphoria; or selling or sharing medication (drug diversion).

- An interim history and physical examination may identify a new diagnosis, including new psychological diagnoses or stressors, or escalation of symptoms leading to inappropriate escalation of medications.
- Patients with stable chronic pain generally do not develop tolerance to a stable regimen or tolerance occurs slowly over time. Inquiries about prescription of a new medication, an increase in tobacco use, or a change in how medication is being taken may explain the patient's altered response.
- If pain is inadequately treated and the patient is experiencing pseudoaddiction, an increase in dosage or a shift to a longer-acting medication with rescue dosages

should result in improved function, decrease in pain scores, and abatement of ADRB.
- Search the state PMP (if available in your state) for doctor shopping, additional psychoactive medication prescriptions, or evidence of prescription fraud.
- If the patient is seeking euphoria, evidence on the physical exam of nasal excoriation related to insufflation, fresh needle marks, and random requests to come to clinic may reveal mental status changes.

Sharing or selling medication may be accompanied by other ADRBs, including use of illicit substances identified on UDT, erratic clinic attendance, or a change in mental status. These may be identified though random requests for pill counts and UDT. If the clinic imposes too many restrictions on a patient who is diverting medication, the patient may voluntarily seek medications elsewhere. The goal of risk assessment and monitoring is not to be punitive or to avoid treating complex patients, but to protect vulnerable patients who may abuse these medications or combine them with illicit drugs, increasing the risk of unintentional overdose.[19] This practice also protects the clinician from medicolegal exposure and the community from exposure to diverted opioids. If the patient refuses to comply with established standards or refuses referral to a chemical dependency program, discharge from the practice may be warranted.

Case study IV

- A 74-year-old female with 5 previous back surgeries has chronic pain and is prescribed methadone and uses oxycodone for breakthrough pain. When she comes alone for an office visit, her pain is better with methadone only and she does not request oxycodone. When her son accompanies her to a visit, she insists on oxycodone prescriptions along with methadone. She has not shown up for pill counts on at least 3 occasions. The prescribing physician believes that this patient needs treatment and methadone is sufficient and that her son may be using or diverting medications.

What is happening in this situation and how should it be managed? This is a high-risk situation for the patient and threatens her care. Failure to show for a random UDT and pill count on 3 separate occasions is especially concerning, particularly if the patient is otherwise adherent to clinic policies. Given her age she may be at risk for victimization,[12] and if psychological consultation is not available in the clinic, discussion of the case with a social worker is appropriate. When the patient arrives alone, asking her directly if she is pressured to share medication may reveal fears and concerns about any changes in prescription. Shortening the time between appointments and dispensing smaller amounts of medication will keep the patient in more frequent contact with the medical system. Until the situation is resolved, discharge should be avoided but oxycodone should be discontinued.

The expert panel discussed many tools for comprehensive risk assessment:

Urine drug screening. As the abuse and misuse of opioids and other prescription drugs has reached alarming levels, monitoring opioid use is crucial for responsible pain management.[2] In treating patients with chronic opioids, utilizing urine drug testing is a mainstay in the monitoring process. In a review of the Database of State Laws, Regulations, and Other Government Policies guidelines of the use of controlled substances in pain management, 23 states recommend UDT and 21 states did not mention UDT, but most of these states recommended ongoing monitoring; 6 states had no policy.[20] According to the Institute for Clinical Systems Improvement, it is recommended that, even with the involvement of a pain specialist, PCPs still should ensure the responsible use of opioids through treatment agreements and UDT.[21]

Peppin et al[22] list a number of additional recommendations for the use of UDT in patients taking opioids. All patients taking a short- or long-acting opioid for 3 months or longer should be tested. Monitoring should consist of a comprehensive UDT that can detect illicit drugs as well as commonly prescribed opioids and other medications of potential abuse. When interpreting the results of UDT, consider the patient history and type of opioid therapy, among other factors. Presence of an illicit drug test, with gas or liquid chromatography/mass spectrometry (GC/MS or LC/MS/MS) confirmation, may indicate that active substance abuse or dependence is present. Additionally, a UDT positive for illegal drugs or medications not prescribed undermines physician-patient trust and jeopardizes the therapeutic relationship. Individuals engaged in substance abuse and addiction place the physician at risk for diversion of their prescriptions because this implies contact with the illicit drug trade. Finally, diversion of psychoactive medications poses a public health risk for accidental overdose deaths. The patient's pain cannot be treated effectively in the face of illicit drug use without addressing the diagnosis of addiction.[14] This group of experts recommended obtaining at least 2 UDTs per year for patients at low risk for abuse and 4 times per year for patients considered to be at high risk for abuse. However, seasoned pain physicians who have a close and long-standing relationship with a patient may not feel it necessary to obtain UDT unless there is a substantial change in behavior.

There currently is no UDT that is considered to be standard for all clinical situations. The 2 current forms of testing are immunoassay (typical for point-of-care testing) and high-performance chromatography/mass spectrometry (typical for confirmatory testing).[23] Random pill counts, adherence checklists, and instruments such as the Screener and Opioid Assessment for Patients with Pain also may be used to assist with the monitoring of adherence.[24]

Screening tools for ADRBs. A variety of screening tools have been developed based on the literature regarding ADRBs that are suggestive of possible opioid misuse or abuse. Screening tools have been designed to prescreen patients prior to initiating opioids and to monitor patients who are currently using opioids. Examples of prescreening tools include the Opioid Risk Tool,[25] Screener and Opioid Assessment for Patients with Pain,[26] Diagnosis, Intractability, Risk, Efficacy,[27] and Drug Abuse Screening Test.[28] Tools used for monitoring patients currently receiving prescription opioids include Pain Assessment and Documentation Tool,[29] and the Current Opioid Misuse Measure.[30] Selecting the most appropriate tool depends on the needs of the practice setting (brief versus comprehensive).

Medical record audit. Although it is not often listed in risk assessment, it is good practice to request medical records for a patient who is new to your practice before initiating opioids or continuing to prescribe opioids initiated by another physician. For example, a new patient arrives at your clinic, having recently moved to your community, with no medical records or test results. The patient has a history of chronic low back pain (LBP) and has been using oxycodone 10 mg 4 times daily. The patient presents a 1-page letter from his or her PCP listing various diagnoses including LBP. The prescribed medications listed include oxycodone, prescribed by a pain specialist. Options include not prescribing any opioids until the patient produces full records from the PCP and pain clinician or obtaining point-of-care UDT and, if appropriate, prescribing a limited, 1-week supply. The patient is informed that 1 further refill will be provided until records are received and reviewed.

Psychological screening. The expert panel agreed that physicians do not use psychological screenings often, as they may not have the appropriate expertise to manage the problems they identify or may have limited access to mental health providers. Psychiatric comorbidities are often seen in patients with a substance use disorder and in patients with chronic pain. Opioids have anxiolytic[31] and possible antidepressant properties,[32] which may lead to abuse/misuse in patients with undertreated depression and/or anxiety. There are a number of brief depression and anxiety screening tools that can be utilized effectively in a busy practice setting.[7] If access to mental health services is limited, use of office-based interventions may be efficacious. For example, Kroneke[33] developed a protocol to treat pain and depression in a primary care setting utilizing an algorithm to maximize antidepressant therapy in combination with a self-taught pain management program. Both pain and depression improved and the changes were maintained for up to 1 year.

Sleep assessment. A sleep assessment may be indicated for patients with chronic pain in general and particularly for patients suffering from both pain and addiction. There is a small but growing body of literature that has documented the association between the use of several illicit drugs and sleep disorders; the vast majority of alcoholic patients entering treatment also have developing sleep disorders. Even when used appropriately, alcohol and opiates can interrupt sleep by increasing wakefulness and decreasing total sleep time, slow-wave sleep, and REM sleep.[34] The Pittsburgh Sleep Quality Index is a validated, self-administered questionnaire used to measure sleep quality. It is a 7-item questionnaire (sleep duration, sleep efficiency, sleep latency, sleep disturbance, daytime dysfunction, frequency of sleep medications, and subjective sleep quality) with each item rated on a scale from 0 to 3.[35] If sleep apnea is suspected, referral to a sleep center for testing is important, especially if a patient is prescribed opiates related to risk of respiratory depression.[36,37]

Assessment of function. Continuing opioid therapy should be determined, in part, by improvement in function after opioids have been prescribed or dosage increased. Function can be assessed utilizing the Brief Pain Inventory,[38] the 6-minute walk test,[39] or other patient self-reporting methods.

Pill counts and reports from drug monitoring databases. Various methods for monitoring medication adherence can play a part in continual risk assessment. Data are emerging that state PMPs may be effective in decreasing the diversion of controlled substances by improving clinical decision making at the point of care. Broader clinician access to PMP databases may help monitor and even improve public health outcomes in terms of safety. Well-designed PMPs can have a critical role in the reduction of opioid abuse, diversion, and overdose.[40] Pill counts are another form of monitoring for opioid patients. Manchikanti et al demonstrated that not only do pill counts help to evaluate the use of prescribed opioids, they also can be a part of an adherence monitoring program to decrease opioid abuse.[41]

Patient stratification

One of the goals of the initial assessment of a pain patient is to stratify the patient into a level of care that is appropriate for their level of risk of abuse. Gourlay, Heit, and Almahrezi[16] and the expert panel suggest the following schematic for stratification:

Group I—primary care patients (low risk). This group has no past or current history of substance abuse disorder (SUD). They have a noncontributory family history with respect to SUDs and lack major or untreated psychopathology. This group clearly represents the majority of patients who will present to the PCP.

The patient may present with discrepant pill counts or openly admit to taking extra medication for rescue purposes. Patients in this category may require motivational interviewing, additional telephone support, and consultation. Close follow-up plans should be set, including more frequent visits.

Group II—primary care patients with specialist support (medium risk). In this group, there may be a past history of SUD or a strong family history of problematic drug use. They also may have co-occurring moderate psychiatric disorder. Although not actively addicted, these patients do represent increased risk that may be better managed in consultation with appropriate specialist support. This consultation may be formal and ongoing or simply provide the option for referral back for reassessment should the need arise.

The physician needs to discuss the situation with the patient, and may have to set clear limits and outline expectations including consequences or problem behaviors. The patient should be aware that the physician may decide to discharge them from the practice, refer them to treatment for substance abuse or addiction, or provide only non-opioid therapy. Specific written suggestions of treatment resources for referral or comanagement should be provided to the patient and documented upon discharge.

Group III—specialty management (high risk). This group of patients represents the most complex cases to manage because of an active SUD or major untreated psychiatric disorder. These patients are actively addicted and pose significant risk to both themselves and to the practitioners, who often lack the resources or experience to manage them.

Patients may present with physical signs of substance use including fresh injection marks, excoriations from stimulant abuse, signs of nasal insufflation, intoxication, or evidence of drug withdrawal. A review of the state PMP reports may indicate that the patient has been prescribed other psychoactive drugs or is seeing multiple physicians for pain medication. These patients cannot be treated for comorbid SUDs by the PCP or pain physician, and may need an immediate referral to inpatient detoxification, residential or intensive outpatient treatment, community mental health center or, if medically unstable, to the emergency department.

It is important to note that reassessments must occur over time, as these categorizations are dynamic, not static.

Strategies and Recommendations for Management of the Addicted Patient

Consider the following case study to guide you through the treatment options that follow:

Case study V: cocaine addiction and severe pain

- After 2 previous lumbar fusions, a 55-year-old female develops severe back and leg pain and is unable to walk. As a result, she is wheelchair bound. Examination of her MRI and X-ray reveals spinal stenosis above the 2 previous fusions. The surgeon rules out further surgery and recommends pain management. Routine UDT confirms cocaine use. The patient denies cocaine use. She is not interested in spinal interventions, physical therapy, or adjunctive medications and wants only opioids. Her prescribing physician required a consultation with an addiction specialist and arranged an appointment. She did not keep the appointment on 3 occasions.

What other testing should the physician order? Mass spectrometry confirmation of the point-of-service cocaine positive result is important. Several prescribed medications and over-the-counter medications can result in a false positive result for many substances. For example zolpidem, coca leaf tea, salicylates, and fluconazole can cause a false positive for cocaine.[22]

What are the options for the patient? By not attending the consultation with the addiction specialist, the patient has indicated that she is unable or unwilling to be adherent to the recommendations of the prescribing physician. She should not be prescribed any controlled medications until she has completed an evaluation. A prescription for opioids with a rapid weaning schedule can be provided to minimize withdrawal symptoms.

What are the options available for the prescribing physician? If the patient is willing to talk with the addiction specialist, a straightforward discussion of the need for treatment of substance abuse can be communicated. The medical contraindications to cocaine use in the face of pain treatment should be communicated; these include decreased vascular supply to tissue, cardiovascular compromise, unintentional overdose, and a concern about diversion while obtaining an illicit drug.

Opioid treatment guidelines from the Substance Abuse and Mental Health Services Administration (SAMHSA) state that opioid treatment programs must provide adequate testing or analysis for drugs of abuse, including at least 8 random drug abuse tests per year, per patient in maintenance treatment, in accordance with generally accepted clinical practice.[42] Peppin et al recommend the following for UDI for low- and medium-risk patients on chronic opioid therapy[22]:

> Low risk—Patients may be periodically eligible for monitoring at each visit, with a minimum of 1 test conducted every 6 months. If point-of-care testing is used, at least 1 comprehensive GC/MS or LC/MS/MS may be conducted yearly.
> Medium risk—Patients may be periodically eligible for monitoring at each visit, with a minimum of 1 test conducted every 3 months. If point-of-care testing is used, at least 1 comprehensive GC/MS or LC/MS/MS test may be conducted every 6 months.

When illicit drugs appear in UDT. The appearance of illicit drugs can be indicative of many situations, including abuse or addiction to the illicit drug; the patient is seeking additional pain relief; the patient is self-medicating; the prescribed drug is being exchanged for an illicit drug; or a lab error/false positive. When an illicit drug appears in a UDT, the lab results should be confirmed by GC/MS if point-of-care testing was used and a follow-up appointment should be scheduled with the patient. The patient should be interviewed in a nonjudgmental, nonpunitive fashion while reviewing the results of the test. Counseling should be provided and another UDT should be administered. Based on the results of the interview, the physician may decide to change therapy, discontinue opioids, or discharge the patient from the program, according to practice protocol.[14]

When prescribed opioid drug serum concentrations are inappropriate. Current state guidelines for the prescription of opioids for chronic pain and the monitoring process tend to borrow from the Institute for Clinical Systems Improvement guidelines for the management of chronic pain. If the patient is abusing or misusing drugs, taper the patient off opioid therapy and consider the involvement of an addiction specialist. To monitor compliance, random UDTs are conducted to check for diversion, drug abuse, and to test for the presence of the drug. If it is found that the patient is noncompliant or abuse is present, taper the patient off the opioid and refer the patient to a physician who specializes in addiction medicine or addiction psychiatry.[21]

Recommended therapeutic approaches

Interventional pain management. Interventional pain management may serve as an acceptable method of treating patients with pain who are addicted or abusing opioids. However, there is some debate regarding the long-term efficacy of interventional treatments, such as in the example of LBP.[43–45]

The following are current options for such management for addicted pain patients:

- Epidural steroid injection may help extremity pain and neurogenic claudication secondary to radiculopathy, degenerative disc disease or spinal stenosis.
- Axial back pain related to facet disease may respond to radiofrequency neurotomy of medial branch nerves.
- Sympathetic blocks may help relieve the pain of complex regional pain syndrome.

- Spinal cord stimulation (SCS) also will help chronic extremity and spine pain that fails to respond to other treatments. Prior to being considered for an SCS trial, patients typically are required to undergo a psychological evaluation to ensure that the patient has an adequate understanding of the procedure, realistic expectations of outcome, and does not have a mood disorder that would interfere with a positive outcome.
- Sacroiliac joint injections help with buttock pain.
- Interventional pain management also is an excellent way to treat addicted patients for acute exacerbating pain.

Nonpharmacologic treatment. For physicians who practice in rural areas or who have poor access to specialty referrals, nonpharmacologic treatment for chronic pain can serve as an effective alternative. Familiarity with the spectrum of resources in a community, specifically alternative practitioners and their modalities of treatment, is important in the care of chronic pain patients with co-occurring SUDs.

Complementary and alternative medicine (CAM). There is currently sparse evidence supporting the use of complementary or alternative interventions for the pain patient diagnosed with SUDs. Nonetheless patients may want to explore CAM and some interventions may be helpful. Acupuncture (one of the most widely used CAM therapies for substance abuse), yoga, and optimal healing environment are some of the many options currently being used and studied in the literature as options for treatment of patients with SUDs.[46,47]

Cognitive behavioral therapy (CBT). There is compelling evidence that supports the efficacy and effectiveness of CBT in the treatment of patients with various pain disorders.[48–51] Similar findings support the use of CBT in the treatment of patients with SUDs.[52–54] Pain patients tend to engage in maladaptive thinking (such as catastrophizing) and behavior (kinesiophobia), which can cause additional suffering and disability. Catastrophizing has been associated with pain intensity and pain-related disability[55] and is a risk factor for suicidal ideation.[56] The basis of CBT is to direct patients to recognize and restructure their view of pain and to identify and reinforce their active role in the process of health restoration. CBT includes specific skill acquisition (relaxation therapy, stress management, cognitive restructuring) followed by skill consolidation and rehearsal, and relapse training.[36] It is important for the practitioner to identify qualified CBT therapists in the community to whom they may refer these complex patients.

Physical therapy. Many physical therapists may not know how to effectively evaluate and treat these complex chronic pain patients. These patients tend to have seen many therapists before and often report a poor response to traditional therapy. Patients need to feel reassured that therapy will not cause more harm or severe pain flares. Informing patients that exercise has been shown to improve both pain and mood[57] may further ease any concerns. The patient must start slowly in therapeutic exercise, build self-confidence, and work with a patient therapist who does not become overwhelmed easily. For primary care and pain physicians, it is important to be familiar with the available physical therapists, and to know how to incorporate them into a comprehensive pain management program.

Treatment of addiction

Community peer support: 12-step programs. "Alcoholics Anonymous is a fellowship of men and women who share their experience, strength, and hope with each other that they may solve their common problems and help others recover from alcoholism."[58]

The first 12-step program, Alcoholics Anonymous (AA), was founded by 2 men suffering from alcoholism, Dr. Bob Smith, a physician, and Bill Wilson. In AA, members learn that the support and encouragement of another member and the knowledge that drinking again will be fatal, bring the opportunity to be in recovery from addiction. Al-Anon was established by Lois Wilson, Bill's wife, to help families of alcoholics and encourages support rather than enabling of the addicted friend or family member. Narcotics Anonymous (NA) is based on the same 12 steps as AA and was established to help those with addiction to other substances. These groups, established in the United States in the twentieth century (now found worldwide), are peer-led, community-based support systems for individuals with SUDs and their families. Twelve-step programs emphasize service to the recovering community, sponsorship, incorporate recognition of spirituality through a higher power of the individual's choice, are open to anyone who desires to stop using alcohol and drugs, and "are not aligned with any specific sect, denomination, organization, politics, or institution."[58] Local 12-step meetings in communities can be located online at <www.aa.org> or <www.na.org>. Some 12-step meetings are designated as "open" so that friends, family, and individuals without addiction can attend. AA, NA, and Al-Anon meetings that are designated as "closed" welcome only individuals directly affected by addiction. All 12-step programs welcome and encourage physicians to attend a meeting, thus understanding this important resource for patients. Every office should have up-to-date lists of local AA, Al-Anon, and NA meetings available for patients. Some physicians working with chronic pain patients with addiction establish a contact within the programs, thus effecting an almost direct "referral." Attending the first 12-step meeting can be overwhelming, and often an active member will fulfill community service requirements by accompanying a newcomer to his or her first meeting.

The Joint Commission has recognized the central role that spirituality plays in the addictive diseases and in their recovery and, since the early 1990s, has mandated that each intake assessment for SUDs include a spiritual assessment.[47] The expert panel agreed that a pure abstinence model for the treatment of chronic pain with co-occurring addiction sometimes is not feasible. Patient participation in the 12-step program, and a focus upon the recovering community, spiritual growth, and sponsorship, is very important in the prevention of relapse for those with chronic pain and SUDs.

Pharmacotherapy. *Non-opioid adjunctive medications for pain control.* The most judicious course of initial intervention for patients with chronic pain and active opioid addiction is

detoxification from the opioids. Pain often can be adequately controlled with use of adjunctive medications. Selection of the type of medication depends on the etiology of the pain. For example, opioids have not been proven efficacious in the treatment of fibromyalgia,[59] a highly prevalent pain syndrome. Tricyclic antidepressants have been used in treating fibromyalgia, and newer antidepressants that have both serotonergic and norepinephrine modulation also have been shown to be efficacious, in particular duloxetine and milnacipran.[60,61]

Antiepileptic drugs also have been recognized as having analgesic effects in certain pain syndromes. For example, pregabalin was approved by the Food and Drug Administration (FDA) for fibromyalgia and the hypothesized mechanism of action is related to modulation of several pain pathway neurotransmitters that have a role in pain processing (glutamate, Substance P).[62] Recent guidelines for managing LBP recommend paracetamol (acetaminophen) and nonsteroidal anti-inflammatory drugs as first-line pharmacologic options for pain control, as well as tricyclic antidepressants.[63]

Neuropathic pain disorders respond well to the antiepileptic drugs (pregabalin and gabapentin), with evidence supporting the efficacy of duloxetine and controlled release paroxetine.[64] Other non-opiate options for pain management include ibuprofen, cyclooxygenase (COX)-2 inhibitors, and aspirin.

General guidelines state that nocioceptive, inflammatory-generated pain disorders respond to both opioids and COX inhibitors; neuropathic pain such as diabetic neuropathy, postherpetic neuralgia, sciatica, and complex regional pain syndrome have been demonstrated in randomized controlled trials to respond to gabapentin, valproate, carbamazepine, lidocaine patch, pregabalin, nortriptyline and desipramine, venlafaxine, and duloxetine, opioids, GABA-agonists, and baclofen.[65,66]

Medication-assisted therapy. Some patients with chronic pain and active addiction will require stabilization of addiction before pain can be adequately treated. The chaos and physiological disruption that ensues when psychoactive substances are regularly used, abused, or addiction is present may adversely affect treatment. Appointments may be missed, finances affected, and employment/insurance coverage lost as addiction becomes a central focus. At a minimum, adherence to medication regimen may be disrupted and substances (licit and illicit) may affect metabolism of prescribed medications. Because prescribed medications are valuable when sold illicitly, patients may "trade" part of their medication for illicit substances. When called for a random pill count, patients may "borrow" identical medication from another patient in the clinic or someone with whom they share pills. Patients abusing or addicted to prescription sedative hypnotics or amphetamines, alcohol, cannabis, tobacco and/or illicit drugs (eg, cocaine, heroin, amphetamines, hallucinogens) should be referred to an addiction medicine or addiction psychiatry physician for treatment. When there is obvious information about diversion, physicians should inform the patient that they are no longer able to prescribe controlled substances. In cases where there is concern, a phone consult with an addiction physician with documentation and continued surveillance is indicated. Tapering a patient off medication may be indicated. Patients with chronic pain who have been identified as abusing or addicted to opioids should be referred to a local opioid treatment program (OTP) or Office-Based Opioid Treatment (OBOT). They may continue to be treated for pain with non-opioid medications and nonpharmaceutical agents; however, they are at risk for overdose, with medication at risk for diversion, until opioid addiction is adequately treated.

There are currently 2 available medications, methadone and buprenorphine, for medication-assisted treatment of opioid addiction and both are prescribed under legal restrictions. Physicians have been barred from prescribing opioids for the treatment of opioid addiction outside a federally recognized OTP since the passage of the Harrison Act in 1914. In 2000, the Drug Abuse Treatment Act (DATA) that was authorized by the US Congress allows the prescription of Class III, IV, and V opioids for addiction in a non-OTP setting, such as a private office or clinic.[67] This is also known as OBOT. However, according to DATA, physicians must complete an 8-hour specialized training course, be assigned a specific Drug Enforcement Agency number, and adhere to treating only a limited number of patients. The only Class III opioid authorized by DATA for opioid addiction is buprenorphine. Buprenorphine is dispensed as a combination tablet with naloxone and is administered sublingually. The available strengths are buprenorphine 8 mg/naloxone 2 mg and buprenorphine 2 mg/naloxone 0.5mg. The monotherapy containing only buprenorphine is sometimes prescribed during pregnancy. Neither buprenorphine nor methadone is FDA approved for use in pregnancy; however, growing evidence indicates treatment with medication is superior to continuing opioid abuse or addiction during pregnancy.[68]

Methadone, originally developed for the treatment of pain, is effective for the treatment of opioid addiction by ameliorating the strong physiologic effects of withdrawal ("cravings"), thus allowing an individual to focus on the work of recovery. This can *only* be prescribed for the treatment of opioid addiction in an OTP. In such a setting individuals must meet specific criterion for admission, are required to attend the clinic daily to receive dosages for the first 3 months, and are closely monitored with UDT. OTP patients are required to attend individual, and sometimes group, counseling. "Take home" dosages are provided to the patient who is adherent to treatment. Regulations for OTP vary by state, as do policies and procedures of differing programs. Physicians can become familiar with OTP in their region by calling the substance abuse and mental health section of the state health department. It may be difficult to identify the patient who is concurrently prescribed methadone through an OTP. This is because some state PMPs are not required to report patients prescribed methadone through an OTP because of the associated stigma. Physicians treating chronic pain are encouraged to become acquainted with the physician director of the OTP in their home community. The complex pharmacological characteristics of methadone, specifically the long half-life of more than 48 hours and interaction with other medications such as alcohol and benzodiazepines, warrant very close attention when prescribed. There has been an increase in prescription overdose deaths wherein methadone is identified on toxicology, usually in concert with other prescription medications, alcohol, and illicit drugs.[69–72] In some decedent cases,

the individual was prescribed opioids, including methadone, which was identified on toxicology. In others, medication had been diverted from prescriptions for pain as well as opioid addiction treatment.

Necessary resources for physicians. Basic resources for treating patients can be found through organizations such as the American Society of Addiction Medicine (<www.asam.org>) and the Physician Clinical Support System (<http://www.aaap.org/buprenorphine/pcss-b>).

Referrals can be completed through the use of telemedicine and computer-assisted CBT. Continuing medical education through professional organizations and professional networking can reveal potential referrals, specialists, and other opportunities for comanagement. If a physician has an addicted patient, resources for AA and NA meetings can be found at <www.aa.org> and <www.na.org>.

Engaging family and social support for those who are addicted can be an important tool for successful recovery. Although success has been seen in the utilization of social support, it accounts for only a small percentage of the variance in drug/alcohol-related outcomes; further research is required in the area.[73]

Conclusion

The treatment of opioid addicted patients and patients at risk of addiction in the presence of CNCP has been proven to be both difficult and controversial. Based on current literature and the suggestions of the expert panel, there are a number of steps physicians can take in order to provide the best care possible for their pain patients. Risk stratification and continuous assessment will help to guide physicians to the level of care required for each patient. UDT, medical record audits, and others are among the many tools that can be utilized to monitor patients on or considered for chronic opioid therapy. Recommendations for how to proceed with patients who are abusing or misusing prescription or illicit drugs should be based on the patient's risk stratification. In addition to pharmacological therapy, physicians should be very familiar with the available nonpharmacological therapies and outside resources that can be built into a patient's treatment plan.

Author Disclosure Statement

The authors declared no conflicts of interest with respect to the research, authorship, and/or publication of this article. Funding for this project was provided by Ameritox, Ltd. to the Jefferson School of Population Health (JSPH), which provided administrative and manuscript support. Dr. Reddy initiated the idea for this article and served as the project chair. Additional expert panel members were selected by Ameritox based on their expertise in the field of pain management and/or management of addicted patients. The expert panel members and JSPH held a telephone conference on November 5, 2012 for a 1-hour kick-off meeting and on December 1, 2012 for 3 hours to discuss current literature on the present subject, gaps in the literature, and how the expert panel would advise clinicians about pain management in the addicted population. JSPH organized and moderated both conference calls for the project; the discussions and recommendations from the December call are summarized in this article.

References

1. Solis K. Ethical, legal, and professional challenges posed by "controlled medication seekers" to healthcare providers, part 2. *American Journal of Clinical Medicine*. 2010;7(2):86–92.
2. Solanki DR, Koyyalagunta D, Shah RV, Silverman SM, Manchikanti L. Monitoring opioid adherence in chronic pain patients: Assessment of risk of substance misuse. *Pain Physician.* 2011;14(2):E119–E131.
3. Breuer B, Cruciani R, Portenoy RK. Pain management by primary care physicians, pain physicians, chiropractors, and acupuncturists: A national survey. *South Med J.* 2010;103(8):738–747.
4. Upshur CC, Luckmann RS, Savageau JA. Primary care provider concerns about management of chronic pain in community clinic populations. *J Gen Intern Med*. 2006;21(6):652–655.
5. Oliver J, Coggins C, Compton P, et al. American Society for Pain Management nursing position statement: Pain management in patients with substance use disorders. *Pain Manag Nurs.* 2012;13(3):169–183.
6. Substance Abuse and Mental Health Services Administration. Results from the 2011 National Survey on Drug Use and Health: Mental Health Findings. Available at: <http://www.samhsa.gov/data/NSDUH/2k11MH_FindingsandDetTables/2K11MHFR/NSDUHmhfr2011.htm>. Accessed January 18, 2013.
7. Cheatle MD, O'Brien CP. Opioid therapy in patients with chronic noncancer pain: Diagnostic and clinical challenges. *Adv Psychosom Med*. 2011;30:61–91.
8. Ives TJ, Chelminski PR, Hammett-Stabler CA, et al. Predictors of opioid misuse in patients with chronic pain: A prospective cohort study. *BMC Health Serv Res.* 2006;6:46.
9. Fishbain DA, Cole B, Lewis J, Rosomoff HI, Rosomoff RS. What percentage of chronic nonmalignant pain patients exposed to chronic opioid analgesic therapy develop abuse/addiction and/or aberrant drug-related behaviors? A structured evidence-based review. *Pain Med*. 2008;9:444–459.
10. Boscarino JA, Rukstalis MR, Hoffman SN, et al. Prevalence of prescription opioid-use disorder among chronic pain patients: Comparison of the DSM-5 vs. DSM-4 diagnostic criteria. *J Addict Dis.* 2011;30(3):185–194.
11. Drug Enforcement Administration. Drug fact sheet: Hydrocodone. Available at: <http://www.justice.gov/dea/druginfo/drug_data_sheets/Hydrocodone.pdf>. Accessed January 4, 2013.
12. Substance Abuse and Mental Health Services Administration. Results from the 2011 National Survey on Drug Use and Health: Summary of national findings. Available at: <http://www.samhsa.gov/data/nsduh/2k11results/nsduhresults2011.htm>. Accessed January 3, 2013.
13. American Society of Addiction Medicine. Definition of addiction. Available at: <http://www.asam.org/for-the-public/definition-of-addiction>. Accessed December 13, 2012.
14. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-TR*. Arlington, VA: American Psychiatric Publishing, Inc.; 2000.
15. Substance Abuse and Mental Health Services Administration (SAMHSA). Substance Abuse Treatment Advisory. Prescription medications: Misuse, abuse, dependence, and addiction. Available at: <http://store.samhsa.gov/shin/content//SMA12-4175/SMA12-4175.pdf>. Accessed December 13, 2012.

16. Gourlay DL, Heit HA, Almahrezi A. Universal precautions in pain medicine: A rational approach to the treatment of chronic pain. *Pain Med*. 2005;6(2):107–112.
17. Starrels JL, Becker WC, Alford DP, Kapoor A, Williams AR, Turner BJ. Systematic review: Treatment agreements and urine drug testing to reduce opioid misuse in patients with chronic pain. *Ann Intern Med*. 2010;152(11):712–720.
18. Cheatle MD, Savage SR. Informed consent in opioid therapy: A potential obligation and opportunity. *J Pain Symptom Manage*. 2012;44:105–116.
19. Webster LR, Cochella S, Dasgupta N, et al. An analysis of the root causes for opioid-related overdose deaths in the United States. *Pain Med*. 2011;12(suppl 2):S26–S35.
20. University of Wisconsin School of Medicine and Public Health, Department of Biostatistics and Medical Informatics. *Database of State Laws, Regulations and Other Government Policies*. Available at: <http://www.medsch.wisc.edu/painpolicy/matrix.htm>. Accessed January 18, 2013.
21. Institute for Clinical Systems Improvement (ICSI). Assessment and management of chronic pain. Available at: <https://www.icsi.org/_asset/bw798b/ChronicPain.pdf>. Accessed December 13, 2012.
22. Peppin JF, Passik SD, Couto JE, et al. Recommendations for urine drug monitoring as a component of opioid therapy in the treatment of chronic pain. *Pain Med*. 2012;13:886–896.
23. Washington State Agency Medical Directors' Group. Interagency guideline on opioid dosing for chronic non-cancer pain: An educational aid to improve care and safety with opioid treatment. Available at: <http://www.agencymeddirectors.wa.gov/Files/OpioidGdline.pdf>. Accessed December 13, 2012.
24. Department of Veterans Affairs and the Department of Defense. Clinical Practice Guideline for Management of Opioid Therapy for Chronic Pain. Available at: <http://www.healthquality.va.gov/cot/cot_310_sum.pdf>. Accessed December 10, 2012.
25. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the opioid risk tool. *Pain Med*. 2005;6:432–442.
26. Butler SF, Budman SH, Fernandez K, Jamison RN. Validation of a screener and opioid assessment measure for patients with chronic pain. *Pain*. 2004;112(1–2):65–75.
27. Belgrade MJ, Schamber CD, Lindgren BR. The DIRE score: predicting outcomes of opioid prescribing for chronic pain. *J Pain*. 2006;7(9):671–681.
28. Skinner HA. The drug abuse screening test. *Addict Behav*.1982;(4):363–371.
29. Passik S, Kirsh KL, Whitcomb L, et al. A new tool to assess and document pain outcomes in chronic pain patients receiving opioid therapy. *Clin Ther*. 2004;26(4):552–561.
30. Butler S, Budman SH, Fernandez KC, et al. Development and validation of the current opioid misuse measure. *Pain*. 2007;130(1–2):144–156.
31. Drolet G, Dumont EC, Gosselin I, Kinkead R, Laforest S, Trottier JF. Role of endogenous opioid system in the regulation of the stress response. *Prog Neuropsychopharmacol Biol Psychiatry*. 2001;25(4):729–741.
32. Berrocoso E, Sánchez-Blázquez P, Garzón J, Mico JA. Opiates as antidepressants. *Curr Pharm Des*. 2009;15(14):1612–1622.
33. Kroenke K, Bair MJ, Damush TM, et al. Optimized antidepressant therapy and pain self-management in primary care patients with depression and musculoskeletal pain: A randomized controlled trial. *JAMA*. 2009;301(20):2099–2110.
34. Mahfoud Y, Talih F, Streem D, Budur K. Sleep disorders in substance abusers: How common are they? *Psychiatry (Edgmont)*. 2009;6(9):38–42.
35. Buysse DJ, Reynolds CF 3rd, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: A new instrument for psychiatric practice and research. *Psychiatry Res*. 1989;28:193–213.
36. Webster LR, Choi Y, Desai H, Webster L, Grant BJ. Sleep-disordered breathing and chronic opioid therapy. *Pain Med*. 2008;9(4):425–432.
37. Mogri M, Desai H, Webster L, Grant BJ, Mador MJ. Hypoxemia in patients on chronic opiate therapy with and without sleep apnea. *Sleep Breath*. 2009;13(1):49–57.
38. Cleeland CS, Ryan KM. Pain assessment: Global use of the brief pain inventory. *Ann Acad Med Singapore*. 1994;23(2):129–138.
39. Du H, Newton PJ, Salamonson Y, Carrieri-Kohlman VL, Davidson PM. A review of the six-minute walk test: Its implication as a self-administered assessment tool. *Eur J Cardiovasc Nurs*. 2009;8(1):2–8.
40. Morgan L, Weaver M, Sayeed Z, Orr R. The use of prescription monitoring programs to reduce opioid diversion and improve patient safety. *J Pain Palliat Care Pharmacother*. 2013;27(1):4–9.
41. Manchikanti L, Manchukonda R, Damron KS, Brandon D, McManus CD, Cash K. Does adherence monitoring reduce controlled substance abuse in chronic pain patients? *Pain Physician*. 2006;9(1):57–60.
42. Substance Abuse and Mental Health Services Administration. Guidelines for the Accreditation of Opioid Treatment Programs. Available at: <http://www.dpt.samhsa.gov/pdf/OTPAccredGuidelines-2007.pdf>. Accessed November 1, 2012.
43. Cahana A, Mavrocordatos P, Geurts JW, Groen GJ. Do minimally invasive procedures have a place in the treatment of chronic low back pain? *Expert Rev Neurother*. 2004;4(3):479–490.
44. Chou R, Atlas SJ, Stanos SP, Rosenquist RW. Nonsurgical interventional therapies for low back pain: a review of the evidence for an American Pain Society clinical practice guideline. *Spine (Phila Pa 1976)*. 2009;34(10):1078–1093.
45. Chou R, Huffman LH. Nonpharmacologic therapies for acute and chronic low back pain: A review of the evidence for an American Pain Society/American College of Physicians clinical practice guideline. *Ann Intern Med*. 2007;147:492–504.
46. Shwartz M, Saitz R, Mulvey K, Brannigan P. The value of acupuncture detoxification programs in a substance abuse treatment system. *J Subst Abuse Treat*. 1999;17(4):305–312.
47. Wesa KM, Culliton P. Recommendations and guidelines regarding the preferred research protocol for investigating the impact of an optimal healing environment on patients with substance abuse. *Journal of Alternative and Complementary Medicine*. 2004;10(suppl 1):19.
48. Lamb SE, Hansen Z, Lall R, Castelnuovo E, Withers EJ, Nichols V. Group cognitive behavioral treatment for low-back pain in primary care: A randomized controlled trial and cost-effectiveness analysis. *Lancet*. 2010;375:916–923.
49. Thieme K, Flor H, Turk D. Psychological pain treatment in fibromyalgia syndrome: Efficacy of operant behavioral and cognitive behavioral treatments. *Arthritis Res Ther*. 2006;8(4):R121.
50. Keefe FJ, Caldwell DS. Cognitive behavioral control of arthritis pain. *Med Clin North Am*. 1997;81:277–290.

51. Linton SJ. A 5-year follow-up evaluation of the health and economic consequences of an early cognitive behavioral intervention for back pain: A randomized, controlled trial. *Spine (Phila PA 1976).* 2006;31(8):853–858.
52. Holder HD, Cisler R, Longabaugh R, Stout RL, Treno AJ, Zweben A. Alcoholism treatment and medical care costs from Project MATCH. *Addiction*. 2000;95(7):999.
53. Dutra L, Stathopoulou G, Basden SL, Leyro TM, Powers MB, Otto MW. A meta-analytic review of psychosocial interventions for substance use disorders. *Am J Psychiatry*. 2008; 165:179–187.
54. Osilla KC, Hepner KA, Muñoz RF, Woo S, Watkins K. Developing an integrated treatment for substance use and depression using cognitive-behavioral therapy. *J Subst Abuse Treat*. 2009;37(4):412–420.
55. Turner JA, Jensen MP, Warms CA, Cardenas DD. Catastrophizing is associated with pain intensity, psychological distress, and pain-related disability among individuals with chronic pain after spinal cord injury. *Pain*. 2002; 98(1–2):127–134.
56. Edwards RR, Smith MT, Kudel I, Haythornthwaite J. Pain-related catastrophizing as a risk factor for suicidal ideation in chronic pain. *Pain*. 2006;126(1–3):272–279.
57. Hoffman MD, Hoffman DR. Does aerobic exercise improve pain perception and mood? A review of the evidence related to healthy and chronic pain subjects. *Curr Pain Headache Rep*. 2007;11(2):93–97.
58. Alcoholics Anonymous. A brief guide to Alcoholics Anonymous. Available at: <http://www.aa.org/pdf/products/p-42_abriefguidetoaa.pdf>. Accessed January 4, 2013.
59. Painter JT, Crofford LJ. Chronic opioid use in fibromyalgia syndrome: A clinical review. *J Clin Rheumatol*. 2013;19(2): 72–77.
60. Mease PJ, Clauw DJ, Gendreau RM, et al. The efficacy and safety of milnacipran for treatment of fibromyalgia. A randomized, double-blind, placebo-controlled trial. *J Rheumatol*. 2009;36(2):398–409.
61. Mease PJ, Russell IJ, Kajdasz DK, et al. Long-term safety, tolerability, and efficacy of duloxetine in the treatment of fibromyalgia. *Semin Arthritis Rheum*. 2010;39(6): 454–464.
62. Arnold LM, Russell IJ, Diri EW, et al. A 14-week, randomized, double-blinded, placebo-controlled monotherapy trial of pregabalin in patients with fibromyalgia. *J Pain.* 2008;9(9): 792–805.
63. Chou R. Pharmacological management of low back pain. *Drugs*. 2010;70(4):385–402.
64. Namaka M, Leong C, Grossbern TA, et al. A treatment algorithm for neuropathic pain: An update. *Consult Pharm.* 2009;24(12):885–902.
65. Woolf CJ, Mannion RJ. Neuropathic pain: Etiology, symptoms, mechanisms and management. *Lancet*. 1999;353:1959–1964.
66. Sindrup SH, Jensen TS. Efficacy of pharmacologic treatments of neuropathic pain: An update and effect related to mechanisms of drug action. *Pain*. 1999;83:389–400.
67. Children's Health Act of 2000. Public L No. 106-310. 114 STAT 1223. (Title XXXV, Section 3502; The Drug Addiction Treatment Act of 2000).
68. Jones HE, Fischer G, Heil SH, et al. Maternal opioid treatment: Human experimental research (MOTHER)—approach, issues and lessons learned. *Addiction*. 2012;107(suppl 1):28–35.
69. Hall AJ, Logan JE, Toblin RL, et al. Patterns of abuse among unintentional pharmaceutical overdose fatalities. *JAMA*. 2008; 300(22):2613–2620.
70. Paulozzi LJ. Drug-induced deaths—United States, 2003–2007. *MMWR Surveill Summ*. 2011;60 suppl:60–61.
71. Warner M, Chen LH, Makuc DM, Anderson RN, Minino AM. Drug poisoning deaths in the United States, 1980–2008. *NCHS Data Brief*. 2011;81:1–8.
72. Wunsch MJ, Nakamoto K, Behonick G, Massello W. Opioid deaths in rural Virginia: A description of the high prevalence of accidental fatalities involving prescribed medications. *Am J Addict.* 2009;18(1):5–14.
73. Dobkin PL, De Civita M, Paraherakis A, Gill K. The role of functional social support in treatment retention and outcomes among outpatient adult substance abusers. *Addiction*. 2002;97(3):347–356.

Address correspondence to:
Dominique Comer, PharmD
Jefferson School of Population Health
901 Walnut Street, 10th Floor
Philadelphia, PA 19107

E-mail: dominique.comer@jefferson.edu